

# DETERMINANTS OF NORMAL MACULAR AND RETINAL NERVE FIBER LAYER THICKNESS MEASURED BY 3D OCT 2000 – TOPCON

Elitsa Hristova<sup>1</sup>, Zornitsa Zlatarova<sup>1</sup>, Klara Dokova<sup>2</sup>

<sup>1</sup>Department of Ophthalmology and Visual Science, Medical University of Varna,  
Specialized Eye Hospital - Varna,

<sup>2</sup>Department of Social Medicine and Health Care Organization, Medical University of Varna

## ABSTRACT

**PURPOSE:** To generate the normative data of macular and retinal nerve fiber layer thickness for Bulgarian population using 3D OCT 2000 – Topcon and to evaluate the effects of gender and age on these parameters.

**MATERIALS AND METHODS:** The 131 eyes of 67 healthy individuals aged between 16-71 years, with no ocular disease and best corrected visual acuity of 20/20, were examined using standard scanning protocols. The mean macular and RNFL thickness were evaluated, and the effects of age and gender on these parameters were analyzed.

**RESULTS:** The mean retinal thickness (RT) was  $275.4 \pm 11.59 \mu\text{m}$ , mean central foveal thickness (CFT) was  $241.8 \pm 2.01 \mu\text{m}$ , mean central point thickness (CPT) was  $213.7 \pm 28.64 \mu\text{m}$ . The macular thickness was lowest at the fovea and maximal at the superior inner macula ( $308.7 \pm 13.6 \mu\text{m}$ ). The mean retinal nerve fiber layer (RNFL) thickness was  $109.44 \pm 9.73 \mu\text{m}$ . The RNFL was thickest in the inferior quadrant ( $136.13 \pm 17.70 \mu\text{m}$ ). There was negative but insignificant correlation between macular thickness and volume, and age. The RNFL thickness showed significant negative correlation with age ( $p=0.03$ ). CFT in females was significantly thinner than in males ( $p=0.01$ ).

**CONCLUSIONS:** Our findings provide basic data to facilitate macular and RNFL thickness analysis using 3D OCT- 2000. The normative database is important for early diagnosis and evaluation of pathological changes in various retinal diseases and glaucoma. Our results indicate that age and gender must be considered while interpreting macular retinal thickness data

**Keywords:** optical coherence tomography; macular thickness; retinal nerve fiber layer; normative

## INTRODUCTION

The introduction of optical coherence tomography (OCT) over the past two decades makes the in-

terpretation and follow-up of retinal diseases much easier. It is non-invasive, high-resolution technique that produces *in vivo* cross-sectional images of tissues that resemble histological analysis (1,2). The spectral domain OCT (SD-OCT) has now superseded time domain OCT (TD-OCT). SD-OCT uses an interferometer with a high speed spectrometer and measures light echoes from all time delay simultaneously rather than sequentially (as in time domain OCT device) thus performing an equivalent of 27,000 A scans/second. Recently, advances in OCT have allowed measurement of the thickness of specific retinal layers, which is useful for diagnosing and monitoring pathological changes in various ocular diseases

### Address for correspondence:

Assoc. Prof. Zornitsa Zlatarova MD, PhD  
Medical University - Varna, Bulgaria  
Department of Ophthalmology and Visual Science  
Specialized Eye Hospital - Varna, Bulgaria  
15 Doyran St. Varna 9002  
Mob: 00359 898 532 083  
e-mail: zzlatarova@abv.bg

**Received:** December 16, 2013

**Accepted:** June 4, 2014

es, including diabetic macular edema (3,4), age-related macular degeneration (5), central serous chorioretinopathy, epiretinal membrane, etc. SD-OCT can also quantify the thickness of the retinal nerve fiber layer (RNFL) providing an objective tool to diagnose glaucomatous axon loss and automatically measure the combined thickness of the three innermost retinal layers (RNFL, ganglion cell layer (GCL), inner plexiform layer (IPL)), which are the most susceptible to early glaucomatous damage. Previous studies using TD-OCT or SD-OCT in healthy eyes reported changes in the macular and RNFL profile in relation to factors such as age and gender (6,7,8,9). Several reports suggest that the macular and retinal nerve fiber thickness varies between ethnic groups (10).

The purpose of our study is to generate the normative data of macular and retinal nerve fiber layer thickness for Bulgarian population using 3D OCT 2000 – Topcon and to evaluate the effects of gender and age on these parameters.

## MATERIALS AND METHODS

This was an observational study of the macular thickness and RNFL thickness in normal eyes as measured by optical coherence tomography. One single operator investigates 131 eyes of 67 healthy volunteers. All of them underwent a complete ophthalmic examination including best-corrected visual acuity estimation, slit-lamp examination, Goldmann applanation tonometry and dilated stereoscopic fundus examination. Exclusion criteria were a BCVA worse than 20/20, refractive error >6.00 diopters sphere and/or 3.00 diopters cylinder, IOP > 21 mmHg, eyes with retinopathy due to any cause, eyes with any characteristic glaucomatous disc change.

Patients were examined using standard scanning protocols: “3D Macula 6.0x6.0mm”, “3D Disc 6.0x6.0mm” and “3D Macula(V) 7.0x7.0mm” with 3D OCT- 2000 [Topcon, Hasunuma-cho, Itabashiku, Tokyo, Japan].

The 3D Macula scanning protocol was with 6.0x6.0mm volume cube scans and 512x128 pixels scan resolution, scan depth 2.3 mm, horizontal resolution 20µm, longitudinal resolution 5-6 µm. Macular thickness was reported in a modified Early Treatment of Diabetic Retinopathy Study, macular map with the central subfield 1 mm in diameter and the inner and outer subfields having diameters of 3mm

and 6mm, respectively. The mean Central Foveal Thickness (CFT), the mean Center Point Thickness (CPT) and the mean macular volume were calculated. At OCT scans central macular thickness was determined automatically and was analyzed by OCT software. In all OCT maps, automated macular thickness detection was performed by instrument’s software analysis without manual operator adjustment.

The RNFL thickness was measured using 3D Disc scanning protocol with 6.0x6.0mm volume cube scans, 512x128 pixels scan resolution, scan depth 2.3mm, horizontal resolution 20 µm, longitudinal resolution 5-6 µm. The RNFL thickness was measured around the disc with 16 averaged consecutive circular B scans with diameter of 3.4 mm and 1024 A scans. The peripapillary RNFL thickness (average and four-quadrant values) was analyzed.

3D Macula (V) scanning protocol with 7.0x7.0mm volume cube scans and 512x128 pixels scan resolution allows three types of thicknesses measuring: Nerve Fiber Layer (NFL), Ganglion Cell Layer (GCL) + Inner Plexiform Layer (IPL), NFL+GCL+IPL. The average thickness of all these layers was calculated.

Associations of macular and RNFL fiber layer measurements with age were examined by Pearson correlation analysis. Age stratified comparisons of all macular and RNFL measurements between genders were carried out using the independent sample t-test or ANOVA. The results were considered to be statistically significant at  $p < 0.05$ . All analysis was performed with SPSS software, version 19.0.

## RESULTS

One hundred thirty-one eyes of sixty-seven normal subjects aged between 16 to 71 years ( $34.86 \pm 13.81$ ) were evaluated. Twenty-nine of them were men – 43% and 38 were women – 57%. The mean retinal thickness (RT) was  $275.4 \pm 11.59 \mu\text{m}$ , mean central foveal thickness (CFT) was  $241.8 \pm 21.01 \mu\text{m}$ , mean central point thickness (CPT) was  $213.7 \pm 28.64 \mu\text{m}$  and mean macular volume was  $7.78 \pm 0.32 \text{ mm}^3$ . The macular thickness was lowest at the fovea and maximal at the superior parafoveal macula ( $308.7 \pm 13.6 \mu\text{m}$ ) (Table 1).

*Table 1. Macular thickness measurements ( $\mu\text{m}$ )*

Parameter	Mean	SD	Range
Fovea	241.83	21.01	197-295
Nasal inner macula	306.49	17.11	212-347
Temporal inner macula	292.90	13.37	256-326
Superior inner macula	308.77	13.67	276-353
Inferior inner macula	300.84	13.82	260-327
Nasal outer macula	283.57	14.92	244-332
Temporal outer macula	256.44	14.80	230-312
Superior outer macula	269.46	13.57	243-309
Inferior outer macula	264.33	13.69	236-304

There was a negative but insignificant correlation between mean RT, mean CFT, mean CPT, mean macular volume and age (Table 2).

*Table 2. Correlation between RT, CFT, CPT, macular volume and age*

Characteristic	Age	
	r	P
Mean RT ( $\mu\text{m}$ )	$275.4 \pm 11.59$	0.060
Mean CFT ( $\mu\text{m}$ )	$241.8 \pm 21.01$	0.295
Mean CPT ( $\mu\text{m}$ )	$213.7 \pm 28.67$	0.608
Mean macular volume ( $\mu\text{l}$ )	$7.78 \pm 0.32$	0.062

poral quadrants ( $76.77 \pm 17.34 \mu\text{m}$ ). The RNFL thickness showed significant negative correlation with age ( $p=0.03$ ). Results for mean NFL thickness, mean thickness of GCL+IPL and mean thickness of NFL+GCL+IPL and also their mean, minimal and maximal thickness in superior and inferior sectors are illustrated in Table 3. There was a negative but insignificant correlation between these parameters and age ( $p=0.88$ ,  $p=0.21$ ,  $p=0.14$ ).

## DISCUSSION

The various models of OCT differ in their mea-

*Table 3. NFL, GCL+IPL and NFL+GCL+IPL thickness*

	Minimal	Maximal	Mean thickness $\pm$ SD
NFL (total)	27	70	$37.04 \pm 5.94$
NFL superior sector	26	69	$35.30 \pm 5.79$
NFL inferior sector	29	71	$38.99 \pm 6.49$
GCL + IPL (total)	59	133	$71.60 \pm 8.02$
GCL + IPL superior sector	57	130	$72.19 \pm 8.12$
GCL + IPL inferior sector	62	136	$70.98 \pm 8.14$
NFL + GCL + IPL (total)	86	179	$107.69 \pm 12.96$
NFL + GCL + IPL superior sector	89	176	$106.95 \pm 10.96$
NFL + GCL + IPL inferior sector	95	182	$109.59 \pm 11.28$

Females were found to have a significant thinner fovea (CFT) as compared to males ( $237.12 \mu\text{m}$ ;  $247.92 \mu\text{m}$  – respectively,  $p=0,01$ ).

The mean RNFL thickness was  $109.44 \pm 9.73 \mu\text{m}$ . The RNFL was thickest in the inferior quadrant ( $136.13 \pm 17.70 \mu\text{m}$ ), followed by superior ( $128.99 \pm 15.24 \mu\text{m}$ ), nasal ( $79.26 \pm 20.71 \mu\text{m}$ ) and tem-

surement of macular thickness due to different retinal segmentation algorithms used (6, 8). Macular thickness measurements are not interchangeable among different instruments. Our goal in this study was to generate normative data for 3D OCT- 2000 es-

timated macular and RNFL thickness and to establish its determinants.

OCT-estimated macular thickness has shown variations between different ethnic groups (8). Asians and African-Americans have thinner maculae when compared to Caucasians. The mean thickness in the central 1mm diameter area was found to be  $176.4 \pm 17.5 \mu\text{m}$  in Chinese,  $181.2 \pm 18.4 \mu\text{m}$  in Indians,  $183.2 \pm 13 \mu\text{m}$  in Thai,  $209.5 \pm 26.7 \mu\text{m}$  in Japanese, and  $212 \pm 20 \mu\text{m}$  in Caucasians (6, 8, 15). In our study macular thickness is least at the fovea and increases in the parafoveal area which is consistent with the normal anatomic contour and confirms the results of other authors (13,14). We found CFT ( $241.8 \pm 21.01 \mu\text{m}$ ) higher than that found in other previous studies (6,11). This difference in the measurements is probably due to the lower mean age of examined subjects. The other reason could also be the fact that different OCT instruments define the inner retinal boundary as the internal limiting membrane (ILM), but they differ in defining the outer retinal boundary and this result in differences in measurements (6). This fact must be kept in mind when interpreting the results and patients should be followed up on the same machine if it's possible.

Our results for the mean RT, mean CFT and their insignificant correlation with age were in contrast with the results by Ooto et al. (11), Koleva-Georgieva et al. (7), Manassakorn et al. (8) and consistent with the studies by Chan et al. (12), Grover et al. (10) and Huang et al. (15) that failed to show a statistically significant association between retinal thickness and age. Our study showed that females had a thinner fovea as compared to males like other similar studies by Song et al. (16) and Massin et al. (17). The thinner fovea in females could probably explain the higher incidence of macular holes in them.

Our results for mean RNFL thickness were higher than the results in similar previous studies by Manassakorn et al. (8) and Budenz et al. (9). The greater thickness could be explained with the fact that RNFL thickness increases with increasing proximity to the optic disc and the measurements were made closer than 3.4-mm diameter around the disc as with Topcon 3D-OCT 2000. Our results supports the ISNT rule by Jonas et al. (18) for maximal RNFL thickness in the inferior quadrant followed by supe-

rior, nasal and temporal quadrants and was consistent with other studies (8). On the contrary, there is a study which shows that the thickness of superior quadrant is higher than the inferior (9). In our study mean RNFL thickness showed significant negative correlation with age in agreement with results by Budenz et al. (9).

Our results did not show a significant correlation between mean NFL thickness, mean thickness of GCL+IPL and mean thickness of NFL+GCL+IPL and age. In contrast, in the study by Ooto et al. (19) the thicknesses of the RNFL, GCL, and IPL correlated negatively with age.

## CONCLUSIONS

Knowledge of the macular thickness and retinal nerve fiber layer thickness in a normal Bulgarian population is important for the evaluation of pathological changes. Our findings provide basic data to facilitate macular and RNFL thickness analysis using 3D OCT- 2000. Our results indicate that age and gender must be considered while interpreting macular retinal thickness data.

## REFERENCES

1. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science*, 1991;254:1178-1181.
2. Chen TC, Cense B, Miller JW, et al. Histologic correlation of in vivo optical coherence tomography-images of the human retina. *Am J Ophthalmol*, 2006;141:1165-1168.
3. Lang G. Optical coherence tomography findings in diabetic retinopathy. *Developments in Ophthalmology*, 2007;39:31-47.
4. Hee M. R., Puliafito C. A., Duker J. S. et al. Topography of diabetic macular edema with optical coherence tomography. *Ophthalmology*, 1998;105(2):360-370.
5. Pieramici D. J., Avery R. L., Ranibizumab: treatment inpatients with neovascular age-related macular degeneration. *Expert Opinion on Biological Therapy*, 2006;6(11):1237-1245.
6. Ooto S, Hangai M, Sacamoto A. Three-Dimensional Profile of Macular Retinal Thickness in Normal Japanese Eyes. *IOVS*, 2010;51(1):465-473.
7. Koleva-Georgieva D, Sivkova N. Assessment of serous macular detachment in eyes with diabetic macular edema by use of spectral-domain opti-

- cal coherence tomography. *Graefes Arch Clin Exp Ophthalmol*, 2009;249(11):1461-1469.
8. Manassakorn A, Chaidaroon W, Ausayakhun S, Aupapong S, Wattananikorn S. Normative database of retinal nerve fiber layer and macular retinal thickness in a Thai population. *Jpn J Ophthalmol*, 2008;52:450456.
  9. Budenz D, Anderson D, Varma R. Determinants of Normal Retinal Nerve Fiber Layer Thickness Measured by Stratus OCT. *Ophthalmology*, 2007;114(6):1046-1052.
  10. Grover S, Murthy RK, Brar VS, Chalam KV. Normative data for macular thickness by high-definition spectral domain optical coherence tomography (Spectralis). *Am J Ophthalmol*, 2009;148:266-271.
  11. Sull AC, Vuong LN, Price LL. Comparison of spectral/Fourier domain optical coherence tomography instruments for assessment of normal macular thickness. *Retina*, 2010;30(2):235-245.
  12. Chan A, Duker JS., Ko TH. Normal Macular Thickness Measurements in Healthy Eyes Using Stratus Optical Coherence Tomography; *Arch Ophthalmol*, 2006;124(2):193-198.
  13. Early Treatment Diabetic Retinopathy Study design and baseline patient characteristics. ETDRS report number 7. *Ophthalmology*, 1991;98(5):741-56.
  14. Loduca AL, Zhang C, Zelkha R, Thickness mapping of retinal layers by spectral-domain optical coherence tomography. *Am J Ophthalmol*, 2010;150(6):849-855.
  15. Huang J, Liu X, Wu Z, Xiao H, Dustin L, Sadda S. Macular thickness measurements in normal eyes with timedomain and Fourier domain optical coherence tomography. *Retina*, 2009;29:980987.
  16. Song WK, Lee SC, Lee ES, Kim CY, Kim SS. Macular thickness variations with sex, age, and axial length in healthy subjects: A spectral domain optical coherence tomography study. *Invest Ophthalmol Vis Sci*, 2010;51:39133918.
  17. Massin P, Erginay A, Haouchine B, Mehidi AB, Paques M, Gaudric A. Retinal thickness in healthy and diabetic subjects measured using optical coherence tomography mapping software. *Eur J Ophthalmol*, 2002;12:102108.
  18. Jonas JB, Budde WM, PandaJoans S. Ophthalmoscopic evaluation of the optic nerve head. *Surv Ophthalmol*, 1999;43:293320.
  19. Ooto S, Hangai M, Tomidokoro A. Effects of age, sex, and axial length on the three-dimensional profile of normal macular layer structures. *Invest Ophthalmol Vis Sci*, 2011;52(12):8769-8779.